? b 155
02sep03 08:23:54 User208669 Session D2361.1
$0.30 0.087 DialUnits File1
$0.30 Estimated cost File1
$0.01 TELNET
$0.31 Estimated cost this search
$0.31 Estimated total session cost 0.087 DialUnits

File 155:MEDLINE(R) 1966-2003/Aug W5
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*File 155: Medline has been reloaded and accession numbers have changed. Please see HELP NEWS 155.

Set Items Description
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? ds
Set Items Description
S1 26715 HEPATITIS(W)C OR HCV
S2 251 NS5B
S3 224 S1 AND S2
S4 86368 NT OR NUCLEOTIDES
S5 35 S3 AND S4
S6 30 H77
S7 17 S1 AND S6
S8 2 MAP AND S3
S9 39 MAP AND S1
S10 953645 DT=REVIEW?
S11 3971 S1 AND S10
S12 2013 S1/TI AND S11
S13 22 S2 AND S12
? t s5/7/26
5/7/26
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
09392401 21157508 PMID: 11257175
Evolutionarily conserved RNA secondary structures in coding and non-coding sequences at the 3' end of the hepatitis G virus/GB-virus C genome.
Cuceanu N M; Tuplin A; Simmonds P
Laboratory for Clinical and Molecular Virology, University of Edinburgh, Summerhall, Edinburgh EH9 1QH, UK.
Journal of general virology (England) Apr 2001, 82 (Pt 4) p713-22, ISSN 0022-1317 Journal Code: 0077340
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Hepatitis G virus (HGV)/GB virus C (GBV-C) causes persistent, non-pathogenic infection in a large proportion of the human population. Epidemiological and genetic evidence indicates a long-term association between HGV/GBV-C and related viruses and a range of primate species, and the co-speciation of these viruses with their hosts during primate evolution. Using a combination of covariance scanning and analysis of variability at synonymous sites, we previously demonstrated that the coding regions of HGV/GBV-C may contain extensive secondary structure of undefined function (Simmonds & Smith, Journal of Virology 73, 5787-5794, 1999). In this study we have carried out a detailed comparison of the structure of the 3'untranslated region (3'UTR) of HGV/GBV-C with that of the upstream NS5B coding sequence. By investigation of free energies on folding, secondary structure predictive algorithms and analysis of covariance between HGV/GBV-C genotypes 1-4 and the more distantly related HGV/GBV-C chimpanzee variant, we obtained evidence for extensive RNA secondary structure formation in both regions. In particular, the NS5B region contained long stem-loop structures of up to 38 internally paired nucleotides which were evolutionarily conserved between human and chimpanzee HGV/GBV-C variants. The prediction of similar structures in the same region of hepatitis C virus may allow the functions of these structures to be determined with a more tractable experimental model.
Record Date Created: 20010321
Record Date Completed: 20010426
? t s7/7/15
7/7/15
DIALOG(R)File 155:MEDLINE(R)
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09485909 21262212 PMID: 11369872
Infectious cDNA clone of the hepatitis C virus genotype 1 prototype sequence.
Lanford R E; Lee H; Chavez D; Guerra B; Brasky K M
Department of Virology and Immunology, Southwest Regional Primate Research Center, Southwest Foundation for Biomedical Research, 7620 NW Loop 410, San Antonio, TX 78227, USA. rlanford@icarus.sfbr.org
Journal of general virology (England) Jun 2001, 82 (Pt 6) p1291-7, ISSN 0022-1317 Journal Code: 0077340
Contract/Grant No.: P51 RR13986; RR; NCRR; U19 AI40035; AI; NIAID
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
A full-length cDNA clone of the hepatitis C virus (HCV) genotype 1 prototype (subtype 1a) sequence was constructed. Synthetic RNA produced from the initial cDNA clone was not infectious following intrahepatic inoculation of a chimpanzee. A consensus clone was prepared by comparison with multiple full-length HCV sequences of genotypes 1, 2 and 3. A total of 11 non-consensus amino acid residues were altered by mutagenesis. Synthetic

RNA from the repaired clone initiated a typical, acute-resolving HCV infection following intrahepatic inoculation of a chimpanzee. In addition, at least one of three chimeric cDNA clones constructed between the HCV-1 and H77 genotype 1a strains of HCV was infectious in a chimpanzee. This is the first example of an infectious chimeric HCV clone. An infectious cDNA clone of HCV-1 will be of particular value, since it is the prototype HCV sequence and many commonly used reagents are based on this sequence.
Record Date Created: 20010522
Record Date Completed: 20010628

? t s7/7/10
7/7/10
DIALOG(R)File 155:MEDLINE(R)
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11013216 97366634 PMID: 9223464
Sequence analysis of the hepatitis C virus genome recovered from serum, liver, and peripheral blood mononuclear cells of infected chimpanzees.
Shimizu Y K; Igarashi H; Kanematu T; Fujiwara K; Wong D C; Purcell R H; Yoshikura H
Department of Hepatitis Virology (SKBB), Faculty of Medicine, University of Tokyo, Bunkyo-ku, Japan.
Journal of virology (UNITED STATES) Aug 1997, 71 (8) p5769-73, ISSN 0022-538X Journal Code: 0113724
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Of 13 different strains of hepatitis C virus (HCV) in the inoculum used, only 1 persisted in human lymphocyte cell lines infected in vitro (N. Nakajima, M. Hijikata, H. Yoshikura, and Y. K. Shimizu, J. Virol. 70:3325-3329, 1996). To determine whether that particular strain (designated H1-2) has a tropism for lymphocytes in vivo, we sequenced hypervariable region 1 (HVR1) of the genome of HCV recovered from the sera, livers, and peripheral blood mononuclear cells (PBMC) of chimpanzees infected with plasma H77, the same inoculum used for the in vitro studies. In the PBMC collected from two chimpanzees during the early phase of infection, H1-2 was detected as the only or predominant HVR1 sequence. H1-2 was also detected in PBMC obtained during persistent infection from a chimpanzee that had been treated with immunosuppressants. From the livers of these chimpanzees, two to six different strains were recovered but H1-2 was not detected. Thus, H1-2 appeared to have an affinity for lymphocytes not only in vitro but also in vivo. In samples collected from a chimpanzee after 6 years of infection, however, such tissue compartmentalization of the HCV genome was not observed; a single strain became predominant in the serum, liver, and PBMC. An HCV strain capable of replicating in both the liver and PBMC probably emerged during in vivo replication and persisted.
Record Date Created: 19970731
Record Date Completed: 19970731

? t s5/7/4-6
5/7/4
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
14691267 22303329 PMID: 12416679
Molecular characterization of a full genome Turkish hepatitis C virus 1b isolate (HCV-TR1): a predominant viral form in Turkey.
Yildiz Esra; Oztan Asli; Sar Funda; Pinarbasi Ergun; Cetin-Atalay Rengul; Akkiz Hikmet; Ozturk Mehmet
Department of Molecular Biology and Genetics and BilGen Genetics and Biotechnology, Research and Development Center, Bilkent University, Ankara, Turkey,
Virus genes (United States) Oct 2002, 25 (2) p169-77, ISSN 0920-8569 Journal Code: 8803967
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Based on direct sequencing information from 5'UTR and NS5B regions, we identified subtype lb as a predominant hepatitis C virus genome in Turkey, which affected more than 91% of 79 patients studied. Next, the full genome sequence of a Turkish lb isolate was obtained by the cloning of polypeptide-encoding region into 7 overlapping fragments. Turkish 1b isolate, which was named HCV-TR1, comprises 9361 nucleotides, including 306 nucleotides of 5'UTR, a single long open reading frame of 9033 nucleotides, and 22 nucleotides of 3'UTR. When compared to HCV lb polypeptide sequences available at GenBank, the predicted polypeptide displayed a total of 36 amino acid substitutions, of which 16 was specific for HCV-TR1 isolate. Despite these changes, major structural and functional motifs of HCV proteins were maintained in HCV-TR1. In contrast, HCV-TR1 displayed amino acid substitutions in 6 out of 9 major cytotoxic T-cell epitopes. These data suggest that HCV-TR1 encodes functionally intact viral proteins, but it also encodes altered viral epitopes, which may affect host immune-response.
Record Date Created: 20021105
Record Date Completed: 20030411

5/7/5
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
13979723 22254830 PMID: 12145289
Modulation of hepatitis C virus RNA-dependent RNA polymerase activity by structure-based site-directed mutagenesis.
Labonte Patrick; Axelrod Vladimir; Agarwal Atul; Aulabaugh Ann; Amin Anthony; Mak Paul; et al
Department of Infectious Disease, Wyeth, Pearl River, New York 10965, USA.

Journal of biological chemistry (United States) Oct 11 2002, 277 (41) p38838-46, ISSN 0021-9258 Journal Code: 2985121R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The hepatitis C virus (HCV) encodes an RNA-dependent RNA polymerase (NS5B), which is indispensable for the viral genome replication. Although structural comparison among HCV NS5B, poliovirus 3D-pol, and human immunodeficiency virus-reverse transcriptase RNA-dependent polymerase reveals the canonical palm, fingers, and thumb domains, the crystal structure of HCV NS5B highlights the presence of a unique A1-loop, which extends from the fingers to the thumb domain (amino acids 12-46), providing many contact points for the proposed "closed" conformation of the enzyme. The polymerase also possesses a tunnel, which starts at the active site and terminates on the back surface of the enzyme. This tunnel of 19 A contains five basic amino acids, which may be engaged in NTP trafficking. In the present study, we exploited the crystal structure of the enzyme to elucidate the involvement of these two structural motifs in enzyme activity by site-directed mutagenesis. As predicted, the replacement of leucine 30 located in the Lambda 1-loop is detrimental to the NS5B activity. Heparin-Sepharose column chromatography and analytical ultracentrifugation experiments strongly suggest a local alteration in the structure of the Leu-30 mutant. An analysis of amino acid substitutions in Arg-222 and Lys-151 within the putative NTP tunnel indicates that Arg-222 was critical in delivering NTPs to the active site, whereas Lys-151 was dispensable. Interestingly, the substitution of lysine 151 for a glutamic acid resulted in an enzyme that was consistently more active in de novo synthesis as well as by "copy-back" mechanism of a self-primed substrate when compared with the wild type NS5B enzyme. Burst kinetic analyses indicate that the gain in function of K151E enzyme was primarily the result of the formation of more productive pre-initiation complexes that were used for the elongation reaction. In contrast to the recent observations, both the wild type and mutant enzymes were monomeric in solution, whereas molecules of higher order were apparent in the presence of RNA template.

Record Date Created: 20021007
Record Date Completed: 20021125

5/7/6
DIALOG(R)File 155:MEDLINE(R)

13975712 22247930 PMID: 12359437

Comparative rates of nucleotide sequence variation in the hypervariable region of E1/E2 and the NS5b region of hepatitis C virus in patients with a spectrum of liver disease resulting from a common source of infection.

Duffy Margaret; Salemi Marco; Sheehy Noreen; Vandamme Anne-Mieke; Hegarty John; Curry Michael; Nolan Niamh; Kelleher Dermot; McKiernan Susan; Hall William W; et al
Department of Medical Microbiology, University College Dublin, Belfield, Dublin, 4, Ireland.

Virology (United States) Sep 30 2002, 301 (2) p354-64, ISSN 0042-6822 Journal Code: 0110674
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The association of the severity of liver disease and the molecular evolution of hepatitis C virus (HCV) during chronic infection remains unclear and controversial. To address this we have studied the interpatient variability in the nucleotide sequence of two regions of the HCV genome, E1/E2, which contain the hypervariable region 1 and the nonstructural NS5b region, in a cohort of Irish female patients who were all recipients of a single source of HCV genotype 1b-contaminated anti-D immunoglobulin in 1977 and 1978 and who over the subsequent 20 years developed a spectrum of liver disease. In addition, quasispecies analysis was used to evaluate intrapatient variability in the E1/E2 region in four patients with mild and four with severe disease. Phylogenetic and evolutionary rate analyses of the nucleotide sequences demonstrated that there was no significant difference between those who developed mild disease and those who had progressed to severe disease or cirrhosis. These findings suggest that other factors, either additional viral or host, may be important in the pathogenesis and clinical outcome of chronic hepatitis C virus infection.

Record Date Created: 20021002
Record Date Completed: 20021104

? t s8/7/1 2
8/7/1
DIALOG(R)File 155:MEDLINE(R)

09014643 20307919 PMID: 10849258

Biochemical and structural analysis of the NS5B RNA-dependent RNA polymerase of the hepatitis C virus.

Lohmann V; Roos A; Korner F; Koch J O; Bartenschlager R
Institute for Virology, Johannes-Gutenberg University Mainz, Mainz, Germany.

Journal of viral hepatitis (ENGLAND) May 2000, 7 (3) p167-74, ISSN 1352-0504 Journal Code: 9435672
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Hepatitis C virus (HCV), the major causative agent of chronic and sporadic non-A, non-B hepatitis worldwide, is a distinct member of the Flaviviridae virus family. These viruses have in common a plus-strand RNA genome that is replicated in the cytoplasm of the infected cell via

minus-strand RNA intermediates. Owing to the lack of reliable cell culture systems and convenient animal models for HCV, the mechanisms governing RNA replication are not known. As a first step towards the development of appropriate in vitro systems, we expressed the NS5B RNA-dependent RNA polymerase (RdRp) in insect cells, purified the protein to near homogeneity and studied its biochemical properties. It is a primer- and RNA template-dependent RNA polymerase able to copy long heteropolymeric templates without additional viral or cellular cofactors. We determined the optimal reaction parameters, the kinetic constants and the substrate specificity of the enzyme, which turned out to be similar to those described for the 3D polymerase of poliovirus. By analysing a series of nucleosidic and non-nucleosidic compounds for their effect on RdRp activity, we found that ribavirin triphosphates have no inhibitory effect, providing direct experimental proof that the therapeutic effect observed in patients is not related to a direct inhibition of the viral polymerase. Finally, mutation analysis was performed to map the minimal NS5B sequence required for enzymatic activity and to identify the 'classical' polymerase motifs important for template and NTP binding and catalysis. (41 Refs.)
Record Date Created: 20000728
Record Date Completed: 20000728

8/7/2
DIALOG(R)File 155:MEDLINE(R)

07717085 93172357 PMID: 7679746
Expression and identification of hepatitis C virus polyprotein cleavage products.
Grakoui A; Wychowski C; Lin C; Feinstone S M; Rice C M
Department of Molecular Microbiology, Washington University School of Medicine, St. Louis, Missouri 63110-1093.
Journal of virology (UNITED STATES) Mar 1993, 67 (3) p1385-95, ISSN 0022-538X Journal Code: 0113724
Contract/Grant No.: CA57973; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hepatitis C virus (HCV) is the major cause of transfusion-acquired non-A, non-B hepatitis. HCV is an enveloped positive-sense RNA virus which has been classified as a new genus in the flavivirus family. Like the other two genera in this family, the flaviviruses and the pestiviruses, HCV polypeptides appear to be produced by translation of a long open reading frame and subsequent proteolytic processing of this polyprotein. In this study, a cDNA clone encompassing the long open reading frame of the HCV H strain (3,011 amino acid residues) has been assembled and sequenced. This clone and various truncated derivatives were used in vaccinia virus transient-expression assays to map HCV-encoded polypeptides and to study HCV polyprotein processing. HCV polyproteins and cleavage products were identified by using convalescent human sera and a panel of region-specific polyclonal rabbit antisera. Similar results were obtained for several mammalian cell lines examined, including the human HepG2 hepatoma line. The data indicate that at least nine polypeptides are produced by cleavage of the HCV H strain polyprotein. Putative structural proteins, located in the N-terminal one-fourth of the polyprotein, include the capsid protein C (21 kDa) followed by two possible virion envelope proteins, E1 (31 kDa) and E2 (70 kDa), which are heavily modified by N-linked glycosylation. The remainder of the polyprotein probably encodes nonstructural proteins including NS2 (23 kDa), NS3 (70 kDa), NS4A (8 kDa), NS4B (27 kDa), NS5A (58 kDa), and NS5B (68 kDa). An 82- to 88-kDa glycoprotein which reacted with both E2 and NS2-specific HCV antisera was also identified (called E2-NS2). Preliminary results suggest that a fraction of E1 is associated with E2 and E2-NS2 via disulfide linkages.
Record Date Created: 19930323
Record Date Completed: 19930323
? t s13/7/2 4-8 10-13
13/7/2
DIALOG(R)File 155:MEDLINE(R)

12001999 99447703 PMID: 10516468
Processing and functions of Hepatitis C virus proteins.
Suzuki R; Suzuki T; Ishii K; Matsuura Y; Miyamura T
Laboratory of Hepatitis Viruses, Department of Virology II, National Institute of Infectious Diseases, Tokyo, Japan. tmiyam@nih.go.jp
Intervirology (SWITZERLAND) Sep 1999, 42 (2-3) p145-52, ISSN 0300-5526 Journal Code: 0364265
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hepatitis C virus (HCV) has a positive-stranded RNA genome of about 9.5 kb and a large open reading frame encoding a precursor polyprotein of ca. 3,000 amino acids (aa). This polyprotein is cleaved by host cellular signalase(s) and viral proteases into 10 viral proteins in the order of NH(2)-Core-E1-E2-p7-NS2-NS3-NS4A-NS4B-NS5A-NS 5B-COOH. Core and E1/E2 are considered to be a capsid protein and envelope glycoproteins, respectively. NS2-NS5B are putative nonstructural proteins involved in the replication of HCV. NS2/3 is a metalloprotease which cleaves in cis at the NS2/3 junction. NS3 possesses serine protease and RNA helicase activities and is responsible for the cleavage of the remaining nonstructural proteins. NS4A is suggested to be a cofactor for NS3 protease. Although the function of p7, NS4B and NS5A are still unknown, an association of a mutation in NS5A with a susceptibility to interferon (IFN) has been reported. NS5B possesses an RNA-dependent RNA polymerase activity. Most of the current findings in

HCV proteins depend on expression studies of HCV cDNA clones because of the lack of an efficient replication system in cell cultures. Therefore, a final assignment of cleavages and functions of HCV proteins has to await the propagation of HCV in cell cultures. (84 Refs.)
Record Date Created: 19991104
Record Date Completed: 19991104

13/7/4
DIALOG(R)File 155:MEDLINE(R)
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11107251 97401438 PMID: 9257244
Review: molecular epidemiology of hepatitis C virus.
Smith D B; Simmonds P
Department of Medical Microbiology, University of Edinburgh, Scotland, United Kingdom.
Journal of gastroenterology and hepatology (AUSTRALIA) Jul 1997, 12 (7) p522-7, ISSN 0815-9319 Journal Code: 8607909
Document type: Historical Article; Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Molecular techniques have been used to investigate the epidemiology of hepatitis C virus (HCV) at several different levels. At a global level, the time of divergence of the diverse HCV genotypes isolated from different geographical regions has been estimated from the rate of divergence observed among a cohort of individuals infected from a common source. Estimates of more than 300 years for virus subtypes and more than 500-2000 years for virus types are consistent with their current geographical distributions. Analysis of virus sequences has also provided evidence for a common source of infection in several large-scale outbreaks of HCV infection, although where there is evidence that the implicated source contains more than one variant it may be difficult to distinguish individuals infected by different sources. Finally, sequence analysis has been used to investigate the vertical or horizontal transmission of HCV between pairs of individuals. The hypervariable region of the E2 gene is the most informative region to study if samples are available soon after the transmission event, but evidence for more distant events can still be obtained from analysis of genes such as NS5b and E1. Interpretation of some studies is complicated by the conservation of the gene region studied, or by the failure to make comparisons with sequences from epidemiologically unrelated viruses. (53 Refs.)
Record Date Created: 19971106
Record Date Completed: 19971106

13/7/5
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
11047251 97401438 PMID: 9257244
Review: molecular epidemiology of hepatitis C virus.
Smith D B; Simmonds P
Department of Medical Microbiology, University of Edinburgh, Scotland, United Kingdom.
Journal of gastroenterology and hepatology (AUSTRALIA) Jul 1997, 12 (7) p522-7, ISSN 0815-9319 Journal Code: 8607909
Document type: Historical Article; Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Molecular techniques have been used to investigate the epidemiology of hepatitis C virus (HCV) at several different levels. At a global level, the time of divergence of the diverse HCV genotypes isolated from different geographical regions has been estimated from the rate of divergence observed among a cohort of individuals infected from a common source. Estimates of more than 300 years for virus subtypes and more than 500-2000 years for virus types are consistent with their current geographical distributions. Analysis of virus sequences has also provided evidence for a common source of infection in several large-scale outbreaks of HCV infection, although where there is evidence that the implicated source contains more than one variant it may be difficult to distinguish individuals infected by different sources. Finally, sequence analysis has been used to investigate the vertical or horizontal transmission of HCV between pairs of individuals. The hypervariable region of the E2 gene is the most informative region to study if samples are available soon after the transmission event, but evidence for more distant events can still be obtained from analysis of genes such as NS5b and E1. Interpretation of some studies is complicated by the conservation of the gene region studied, or by the failure to make comparisons with sequences from epidemiologically unrelated viruses. (53 Refs.)
Record Date Created: 19971106
Record Date Completed: 19971106

13/7/6
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
11014730 97368158 PMID: 9224925
The nonstructural proteins of the hepatitis C virus: structure and functions.
Neddermann P; Tomei L; Steinkuhler C; Gallinari P; Tramontano A; De Francesco R
I.R.B.M-Istituto di Ricerche di Biologia Molecolare P. Angeletti-Pomezia, Rome, Italy.
Biological chemistry (GERMANY) Jun 1997, 378 (6) p469-76, ISSN

1431-6730 Journal Code: 9700112
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The hepatitis C virus is the major causative agent of nonA-nonB hepatitis worldwide. Although this virus cannot be cultivated in cell culture, several of its features have been elucidated in the past few years. The viral genome is a single-stranded, 9.5kb long RNA molecule of positive polarity. The viral genome is translated into a single polyprotein of about 3000 amino acids. The virally encoded polyprotein undergoes proteolytic processing by a combination of cellular and viral proteolytic enzymes in order to yield all the mature viral gene products. The gene order of HCV has been determined to be C-E1-E2-p7-NS2-NS3-NS4A-NS4B-NS5A-NS5B. The mature structural proteins, C, E1 and E2 have been shown to arise from the viral polyprotein via proteolytic processing by host signal peptidases. Conversely, generation of the mature nonstructural proteins relies on the activity of viral proteases. Thus, cleavage at the NS2/NS3 junction is accomplished by a metal-dependent autoprotease encoded within NS2 and the N-terminus of NS3. The remaining cleavages downstream from this site are effected by a serine protease contained within the N-terminal region of NS3. Besides the protease domain, NS3 also contains an RNA helicase domain at its C-terminus. NS3 forms a heterodimeric complex with NS4A. The latter is a membrane protein that has been shown to act as a cofactor of the protease. Whereas the NS5B protein has been shown to be the viral RNA-dependent RNA polymerase, no function has yet been attributed to NS4B and NS5A. The latter is a cytoplasmic phosphoprotein and appears to be involved in mediating the resistance of the hepatitis C virus to the action of interferon. (84 Refs.)
Record Date Created: 19970829
Record Date Completed: 19970829

13/7/7
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
10726990 97076433 PMID: 8918741
Structure, genomic organization, replication and variability of hepatitis C virus.
Pozzetto B; Bourlet T; Grattard F; Bonnevial L
Bacteriology-Virology Laboratory, Faculty of Medicine Jacques Lisfranc, Saint-Etienne, France.
Nephrology, dialysis, transplantation - official publication of the European Dialysis and Transplant Association - European Renal Association (ENGLAND) 1996, 11 Suppl 4 p2-5, ISSN 0931-0509 Journal Code: 8706402
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hepatitis C virus (HCV) is an enveloped, single-stranded RNA virus that has been classified in the Flaviviridae family. The genome of 9400 nucleotides comprises two non-coding regions in 5' and 3' flanking a large reading frame which codes for a polyprotein of 3000 amino acids; this polyprotein is further cleaved into structural (C, E1, E2) and non-structural (NS1, NS2, NS3, NS4, NS5) proteins. The positive RNA acts as a cap-independent messenger; the transcription is mediated by the NS5 RNA polymerase. After the maturation step, the virion is liberated by budding through the cytoplasmic membrane. As for many other RNA viruses, the HCV genome exhibits a high degree of variability, especially in the E2/NS1, E1, NS3 and NS5b regions. Conversely the 5' non-coding region is highly conserved, at least in part, and can be used for diagnostic purposes by PCR technique. Six genotypes of HCV have already been reported, numbered from 1 to 6 in Simmonds' classification. The same genotype can be divided into subtypes (for instance, genotype 1 comprises three subtypes: 1a, 1b and 1c). Various minor variants of the same strain, called quasispecies, are commonly present in the blood of the same patient. Strains of genotype 1b--which is the most widespread worldwide--are correlated with more severe clinical manifestations, greater viral loads and lower response to interferon treatment. The high variability of the HCV genome contributes greatly to the difficulty of designing potent vaccines. (11 Refs.)
Record Date Created: 19970218
Record Date Completed: 19970218

13/7/8
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
10616288 96433905 PMID: 8836884
Processing pathways of the hepatitis C virus proteins.
Lohmann V; Koch J O; Bartenschlager R
Institute for Virology Johannes-Gutenberg-University of Main, Germany.
Journal of hepatology (DENMARK) 1996, 24 (2 Suppl) p11-9, ISSN 0168-8278 Journal Code: 8503886
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hepatitis C virus (HCV) is the major etiological agent of posttransfusion and community-acquired non-A, non-B hepatitis. It is an enveloped virus, grouped as a separate genus in the Flaviviridae family. The plus-stranded RNA genome encodes a polyprotein of about 3000 amino acids with the structural proteins core, E1 and E2 residing in the amino terminal quarter of the polyprotein and the nonstructural proteins NS2, NS3, NS4A, NS4B, NS5A and NS5B in the remainder. Maturation of the structural proteins is mediated by host cell signalases located in the lumen of the endoplasmic reticulum and cleaving behind stretches of hydrophobic amino acids. At

least two virally encoded proteinases are responsible for processing of the NS proteins: a zinc-dependent metallo-proteinase encompassing the NS2 domain and the amino terminal portion of NS3, which is essential for cleavage at the NS2/3 junction; a serine-type proteinase located in the amino terminal domain of NS3 is required for cleavage at all sites downstream of the NS3 carboxy terminus. However, although the NS3 domain contains proteolytic activity, with the exception of the NS5A/5B junction cleavage only occurs in the presence of NS4A. This 54 amino acid long peptide can modulate the proteolytic activity of the enzyme in cis and in trans, probably by the formation of a stable NS3/NS4A complex. Modulation of the proteinase activity may be a way to regulate the expression and replication of the HCV genome. (63 Refs.)
Record Date Created: 19961212
Record Date Completed: 19961212

13/7/10
DIALOG(R)File 155:MEDLINE(R)

09733399 21534724 PMID: 11676530
Recent advances in the molecular biology of hepatitis C virus.
Rosenberg S
Department of Chemistry, University of California, Berkeley, CA 94720, USA. srbchem@pacbell.net
Journal of molecular biology (England) Oct 26 2001, 313 (3) p451-64, ISSN 0022-2836 Journal Code: 2985088R
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The Hepatitis C virus is a positive-stranded RNA virus which is the causal agent for a chronic liver infection afflicting more than 170,000,000 people world-wide. The HCV genome is approximately 9.6 kb in length and the proteome encoded is a polyprotein of a little more than 3000 amino acid residues. This polyprotein is processed by a combination of host and viral proteases into structural and non-structural proteins. The functions of most of these proteins have been established by analogy to other viruses and by sequence homology to known proteins, as well as subsequent biochemical analysis. Two of the non-structural proteins, NS4b and NS5a, are still of unknown function. The development of antivirals for this infectious agent has been hampered by the lack of robust and economical cell culture and animal infection systems. Recent progress in the molecular virology of HCV has come about due to the definition of molecular clones, which are infectious in the chimpanzee, the development of a subgenomic replicon system in Huh7 cells, and the description of a transgenic mouse model for HCV infection. Recent progress in the structural biology of the virus has led to the determination of high resolution three-dimensional structures of a number of the key virally encoded enzymes, including the NS3 protease, NS3 helicase, and NS5b RNA-dependent RNA polymerase. In some cases these structures have been determined in complex with substrates, co-factors (NS4a), and inhibitors. Finally, a variety of techniques have been used to define host factors, which may be required for HCV replication, although this work is just beginning. Copyright 2001 Academic Press. (139 Refs.)
Record Date Created: 20011025
Record Date Completed: 20011204

13/7/11
DIALOG(R)File 155:MEDLINE(R)

09546376 21327286 PMID: 11434427
Molecular virology of hepatitis C virus.
Kato N
Department of Molecular Biology, Okayama University Graduate School of Medicine and Dentistry, Japan. nkato@md.okayama-u.ac.jp
Acta medica Okayama (Japan) Jun 2001, 55 (3) p133-59, ISSN 0386-300X Journal Code: 0417611
Document type: Journal Article; Review; Review, Academic
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hepatitis C virus (HCV), discovered in 1989, is the major causative agent of parenteral non-A, non-B hepatitis worldwide. Following the development of a method of diagnosing HCV infection, it became apparent that HCV frequently causes chronic hepatitis. Persistent infection with HCV is implicated in liver cirrhosis and hepatocellular carcinoma. Current worldwide estimations suggest that more than 170 million people have been infected with HCV, an enveloped positive single-stranded RNA (9.6-kilobases) virus belonging to the Flaviviridae. The HCV genome shows remarkable sequence variation, especially in the hypervariable region 1 of the E2 protein-encoding region, and globally, HCV appears to be distributed with more than 30 genotypes. Complicated "quasispecies" and frequent mutations of viral genomes have also emerged. The HCV genome encodes a large polyprotein precursor of about 3,000 amino acid residues, and this precursor protein is cleaved by the host and viral proteinases to generate at least 10 proteins in the following order: NH2-core-envelope (E1)-E2-p7-nonstructural protein 2 (NS2)-NS3-NS4A-NS4B-NS5A-NS5B-COOH. These viral proteins not only function in viral replication but also affect a variety of cellular functions. Although several explanations have been proposed, the mechanisms of HCV infection and replication in targeted cells, the mechanism of persistent viral infection, and the pathogenesis of hepatic diseases (hepatitis or hepatocellular carcinoma) are all poorly understood. A major reason why these mechanisms remain unclear is the lack of a good experimental HCV replication system. Although several classical trials using cultured cells have been reported, several new, more promising

experimental strategies (generations of infectious cDNA clone, replicon, animal models, etc.) are currently being designed and tested, in order to resolve these problems. In addition, new therapies for chronic hepatitis have also been developed. The enormous body of information collected thus far in the field of HCV research is summarized below, and an overview of the current status of HCV molecular virology of HCV is provided. (358 Refs.)
Record Date Created: 20010703
Record Date Completed: 20011204

13/7/12
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
09383247 21146669 PMID: 11252351
Genome of human hepatitis C virus (HCV): gene organization, sequence diversity, and variation.
Kato N
Department of Molecular Biology, Institute of Cellular and Molecular Biology, Okayama University Medical School, Japan. nkato@med.okayama-u.ac.jp
Microbial & comparative genomics (United States) 2000, 5 (3) p129-51, ISSN 1090-6592 Journal Code: 9616596
Document type: Journal Article; Review; Review, Academic
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hepatitis C virus (HCV) is the major etiologic agent of non-A, non-B hepatitis. HCV infection frequently causes chronic hepatitis, which progresses to liver cirrhosis and hepatocellular carcinoma. Since the discovery of HCV in 1989, a large number of genetic analyses of HCV have been reported, and the viral genome structure has been elucidated. An enveloped virus, HCV belongs to the family Flaviviridae, whose genome consists of a positive-stranded RNA molecule of about 9.6 kilobases and encodes a large polyprotein precursor (about 3000 amino acids). This precursor protein is cleaved by the host and viral proteinase to generate at least 10 proteins: the core, envelope 1 (E1), E2, p7, nonstructural (NS) 2, NS3, NS4A, NS4B, NS5A, and NS5B. These HCV proteins not only function in viral replication but also affect a variety of cellular functions. HCV has been found to have remarkable genetic heterogeneity. To date, more than 30 HCV genotypes have been identified worldwide. Furthermore, HCV may show quasispecies distribution in an infected individual. These findings may have important implications in diagnosis, pathogenesis, treatment, and vaccine development. The hypervariable region 1 found within the envelope E2 protein was shown to be a major site for the genetic evolution of HCV after the onset of hepatitis, and might be involved in escape from the host immunesurveillance system. (240 Refs.)
Record Date Created: 20010316
Record Date Completed: 20010621

13/7/13
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
09381642 21144920 PMID: 11249710
Recent advances in the analysis of HCV NS5B RNA-dependent RNA polymerase.
Lesburg C A; Radfar R; Weber P C
Department of Structural Chemistry, Schering-Plough Research Institute, 2015 Galloping Hill Road, Kenilworth, NJ 07033, USA. Charles.Lesburg@spcorp.com
Current opinion in investigational drugs (London, England - 2000) (England) Nov 2000, 1 (3) p289-96, ISSN 1472-4472 Journal Code: 100965718
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
An RNA-dependent RNA polymerase denoted nonstructural protein 5B (NS5B) is the central enzyme in replication of the hepatitis C virus genome. Recent advances in the biochemical and structural understanding of NS5B include solubilization and purification of the full-length enzyme and various truncated forms. In vitro conditions for NS5B-catalyzed primer elongation using both homo- and heteropolymeric RNA templates were discovered. The crystal structure of the NS5B apoenzyme revealed a globular shape unique among polymerases, and implicated new structural features important for binding the RNA template and cognate ribonucleotide substrates. The crystallographic results also provided a structure-based framework for biochemical analyses and drug-design efforts. Finally, inhibitors of HCV RNA-dependent RNA polymerase have been reported. (47 Refs.)
Record Date Created: 20010315
Record Date Completed: 20010517
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02sep03 08:38:03 User208669 Session D2361.2
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$3.78 18 Type(s) in Format 7
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File 155:MEDLINE(R) 1966-2003/Aug W5
(c) format only 2003 The Dialog Corp.
*File 155: Medline has been reloaded and accession numbers have changed. Please see HELP NEWS 155.

Set Items Description
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? s ns5b
S1 251 NS5B
? s crystal
S2 36268 CRYSTAL
? s s1 and s2
251 S1
36268 S2
S3 12 S1 AND S2
? s hepatitis and s3
110606 HEPATITIS
12 S3
S4 12 HEPATITIS AND S3
? t s4/7/6 7 10
4/7/6
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
11991081 99436521 PMID: 10504728
Crystal structure of the RNA-dependent RNA polymerase from hepatitis C virus reveals a fully encircled active site.
Lesburg C A; Cable M B; Ferrari E; Hong Z; Mannarino A F; Weber P C
Department of Structural Chemistry, Schering-Plough Research Institute, Kenilworth, New Jersey 07033, USA.
Nature structural biology (UNITED STATES) Oct 1999, 6 (10) p937-43, ISSN 1072-8368 Journal Code: 9421566
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Various classes of nucleotidyl polymerases with different transcriptional roles contain a conserved core structure. Less is known, however, about the distinguishing features of these enzymes, particularly those of the RNA-dependent RNA polymerase class. The 1. 9 A resolution crystal structure of hepatitis C virus (HCV) nonstructural protein 5B (NS5B) presented here provides the first complete and detailed view of an RNA-dependent RNA polymerase. While canonical polymerase features exist in the structure, NS5B adopts a unique shape due to extensive interactions between the fingers and thumb polymerase subdomains that serve to encircle the enzyme active site. Several insertions in the fingers subdomain account for intersubdomain linkages that include two extended loops and a pair of antiparallel alpha-helices. The HCV NS5B apoenzyme structure reported here can accommodate a template:primer duplex without global conformational changes, supporting the hypothesis that this structure is essentially preserved during the reaction pathway. This NS5B template:primer model also allows identification of a new structural motif involved in stabilizing the nascent base pair.
Record Date Created: 19991027
Record Date Completed: 19991027

4/7/7
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
11110417 97404652 PMID: 9261364
The hepatitis C virus NS4A protein: interactions with the NS4B and NS5A proteins.
Lin C; Wu J W; Hsiao K; Su M S
Vertex Pharmaceuticals Incorporated, Cambridge, Massachusetts 02139-4242, USA. Lin@vpharm.com
Journal of virology (UNITED STATES) Sep 1997, 71 (9) p6465-71, ISSN 0022-538X Journal Code: 0113724
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hepatitis C virus encodes a large polyprotein precursor that is proteolytically processed into at least 10 distinct products, in the order NH2-C-E1-E2-p7-NS2-NS3-NS4A-NS4B-NS5A-NS5B -COOH. A serine proteinase encoded in the N-terminal 181 residues of the NS3 nonstructural protein is responsible for cleavage at four sites (3/4A, 4A/4B, 4B/5A, and 5A/5B) in the nonstructural region. NS4A, a 54-residue nonstructural protein which forms a stable complex with the NS3 proteinase, is required as a cofactor for cleavage at the 3/4A and 4B/5A sites and enhances processing at the 4A/4B and 5A/5B sites. Recently reported crystal structures demonstrated that NS4A forms an integral part of the NS3 serine proteinase. In this report, we present evidence that NS4A forms a nonionic-detergent-stable complex with the NS4B5A polyprotein substrate, which may explain the requirement of NS4A for the 4B/5A cleavage. Isoleucine-29 of NS4A, which has been previously shown to be essential for its proteinase cofactor activity and formation of the NS3 complex, was found to be important for the interaction between NS4A and the NS4B5A substrate. In addition, two

more hydrophobic residues in the NS4A central region (valine-23 and isoleucine-25) were also shown to be essential for the cofactor activity and for the interaction with either the NS3 proteinase or the NS4B5A polyprotein substrate. Finally, the possible mechanisms by which these viral proteins interact with each other are discussed.
Record Date Created: 19970917
Record Date Completed: 19970917

4/7/10
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
09381642 21144920 PMID: 11249710
Recent advances in the analysis of HCV NS5B RNA-dependent RNA polymerase.
Lesburg C A; Radfar R; Weber P C
Department of Structural Chemistry, Schering-Plough Research Institute, 2015 Galloping Hill Road, Kenilworth, NJ 07033, USA. Charles.Lesburg@spcorp.com
Current opinion in investigational drugs (London, England - 2000) (England) Nov 2000, 1 (3) p289-96, ISSN 1472-4472 Journal Code: 100965718
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
An RNA-dependent RNA polymerase denoted nonstructural protein 5B (NS5B) is the central enzyme in replication of the hepatitis C virus genome. Recent advances in the biochemical and structural understanding of NS5B include solubilization and purification of the full-length enzyme and various truncated forms. In vitro conditions for NS5B-catalyzed primer elongation using both homo- and heteropolymeric RNA templates were discovered. The crystal structure of the NS5B apoenzyme revealed a globular shape unique among polymerases, and implicated new structural features important for binding the RNA template and cognate ribonucleotide substrates. The crystallographic results also provided a structure-based framework for biochemical analyses and drug-design efforts. Finally, inhibitors of HCV RNA-dependent RNA polymerase have been reported. (47 Refs.)
Record Date Created: 20010315
Record Date Completed: 20010517
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$3.55 Estimated cost this search
$3.82 Estimated total session cost 0.625 DialUnits
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02sep03 10:49:34 User208669 Session D2363.1
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$0.29 Estimated cost File1
$0.01 TELNET
$0.30 Estimated cost this search
$0.30 Estimated total session cost 0.083 DialUnits

SYSTEM:OS - DIALOG OneSearch
File 155:MEDLINE(R) 1966-2003/Aug W5
(c) format only 2003 The Dialog Corp.
*File 155: Medline has been reloaded and accession numbers have changed. Please see HELP NEWS 155.
File 357:Derwent Biotech Res. _1982-2003/Aug W5
(c) 2003 Thomson Derwent & ISI
*File 357: File is now current. See HELP NEWS 357.
Alert feature enhanced for multiple files, etc. See HELP ALERT.

Set Items Description
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? ds
Set Items Description
S1 14208 HEPTITIS (W)C OR HCV
S2 27728 HEPATITIS (W)C OR HCV
S3 231058 NS5B OR NS5 OR POLYMERASE
S4 5088 S2 AND S3
S5 243952 FRAGMENT OR FRAGMENTS
S6 382 S4 AND S5
S7 4090 S3(3N)S5
S8 46 S2 AND S7
S9 45 RD (unique items)
S10 390106 PEPTIDE OR PEPTIDES OR OLIGOPEPTIDE OR OLIGOPEPTIDES
S11 323 S4 AND S10
S12 41 S3(3N)S10 AND S4
? t s9/7/28
9/7/28 (Item 28 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
09082723 20379814 PMID: 10923525
[Cloning and expressing of HCV NS5 partial gene and dynamic changes of anti-NS5]

Xu D; Lu H; Niu J
Institute of Basic Medical Sciences, Academy of Military Medical Sciences, Beijing.
Zhonghua yi xue za zhi (CHINA) Mar 1998, 78 (3) p183-6, ISSN 0376-2491 Journal Code: 7511141
Document type: Journal Article ; English Abstract
Languages: CHINESE
Main Citation Owner: NLM
Record type: Completed
OBJECTIVE: To study antigenicity of HCV NS5 protein and dynamic changes of anti-NS5 in post-transfusion hepatitis C (PT-HC). METHODS: Epitopes of HCV NS5 protein were analyzed by Goldkey Program. NS5 gene fragment was amplified by reverse transcription and polymerize chain reaction (RT-PCR) from sera of PT-HC patients. Sequence analysis was performed, and recombinant strain was constructed. Series sera from PT-HC were detected for anti-NS5, ALT and HCV RNA. RESULTS: The homology of nucleotide and amino acid with genotype II in the same region was 91.8% and 92.4%, respectively. SDS-PAGE analysis showed an expressing band around 50 kD, the fusion protein represented about 21.4% of total bacterial protein. Western blot result proved the expressing band could specifically react with sera from hepatitis C patients. Detection results of series blood samples from PT-HC showed that the antibody against NS5 appeared relatively late, the positive conversion time was 182.9 +/- 168.5 day. Dynamic changes of anti-NS5 were correlated with serum ALT in most cases. The types of dynamic change of anti-NS5 were passing positive; intermittent positive; persistent positive, and persistent negative in two years. CONCLUSION: Antibody against NS5 may reflect the disease activity to some extent. It appears relatively late, and is of no value in early stage diagnosis.
Record Date Created: 20000915
Record Date Completed: 20000915
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12/7/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11613862 99046901 PMID: 9831038
DNA-based selection and screening of peptide ligands.
Bartoli F; Nuzzo M; Urbanelli L; Bellintani F; Prezzi C; Cortese R; Monaci P
Istituto di Ricerche di Biologia Molecolare P. Angeletti, Pomezia (Roma), Italy.
Nature biotechnology (UNITED STATES) Nov 1998, 16 (11) p1068-73, ISSN 1087-0156 Journal Code: 9604648
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Phage display selection strategies rely on the physical link between the displayed heterologous protein ligand and the DNA encoding it. Thus, genes expressing a ligand with a specific binding affinity can be selected rapidly. To improve the specificity and sensitivity of this technology for potential use in identifying ligands to a specific antibody present in a complex mixture, we incorporated a DNA selection step along with the phage display technology. Ligands for hepatitis C virus (HCV) antibodies present in serum were identified by panning a phage-displayed random peptide library against pools of serum HCV antibodies. An additional DNA hybridization screening step using single-stranded DNA isolated from one of the pools increased the specificity and sensitivity, resulting in the selection of an HCV antibody ligand with diagnostic potential.
Record Date Created: 19990208
Record Date Completed: 19990208

12/7/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10314703 96116857 PMID: 8537460
Epitope mapping of the NS4 and NS5 gene products of hepatitis C virus and the use of a chimeric NS4-NS5 synthetic peptide for serodiagnosis.
Rosa C; Osborne S; Garetto F; Griva S; Rivella A; Calabresi G; Guaschino R; Bonelli F
Sorin Biomedica, R&D Diagnostic Division, Saluggia (VC), Italy.
Journal of virological methods (NETHERLANDS) Oct 1995, 55 (2) p219-32, ISSN 0166-0934 Journal Code: 8005839
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Specific domains of the NS4 and NS5 gene products of hepatitis C virus have been identified using hydrophilicity profiles for the prediction of potential immunogenic regions, and epitope scanning techniques. Peptides synthesised on the basis of such data show excellent reactivity in the ELISA format. Introduction of a glycine-glycine spacer between two peptides (NS4-12 and NS5-44) to give a single chimeric peptides does not appear to impair immunoreactivity. An ELISA based on the chimeric peptide and a Core-NS3 recombinant protein correctly diagnoses a cohort of haemodialysed patients, three commercial HCV panels and the sera of a negative control population.
Record Date Created: 19960205
Record Date Completed: 19960205

12/7/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10249284 96050825 PMID: 7496964
Antigenic structure of the complete nonstructural (NS) 2 and 5 proteins

of hepatitis C virus (HCV): anti-HCV NS2 and NS5 antibody reactivities in relation to HCV serotype, presence of HCV RNA, and acute HCV infection.
Zhang Z X; Chen M; Sonnerborg A; Sallberg M
Department of Clinical Virology, Huddinge Hospital, Sweden.
Clinical and diagnostic laboratory immunology (UNITED STATES) May 1994, 1 (3) p290-4, ISSN 1071-412X Journal Code: 9421292
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Antigenic regions within the nonstructural (NS) 2 and 5 proteins of hepatitis C virus (HCV) were identified and characterized by the use of 127 overlapping synthetic peptides and a serum panel consisting of 167 human serum samples from persons with antibodies to HCV. Initially, 20 anti-HCV-positive serum samples were used to screen the peptides covering the complete NS2 and NS5 proteins. Among the 27 overlapping peptides spanning the NS2 protein of HCV, only the peptide covering residues 960 to 975 was recognized by human sera. Within the 100 peptides covering the NS5 protein, major linear antigenic regions were located at residues 2284 to 2329 within the putative NS5a and at residues 2584 to 2599 and 2944 to 2959 within the putative NS5b. Additional minor linear antigenic regions were also identified within the NS5. The sequence of the antigenic region of the NS2 protein is, unlike most parts of the NS2 protein, highly conserved among the described types of HCV, whereas the sequence of the major antigenic region of NS5 shows variability among HCV types. The recognition of a peptide corresponding to a part of the major region of NS5 was found to be dependent on HCV type. In 129 anti-HCV-positive serum samples, the prevalence of antibodies to the NS2 protein was found to be 23% among HCV RNA-positive sera and 10% among HCV RNA-negative sera. In the same samples, reactivity to the major linear antigenic regions of HCV NS5 was found in 68% of the HCV RNA-positive sera and 67% of the HCV RNA-negative sera.(ABSTRACT TRUNCATED AT 250 WORDS)
Record Date Created: 19960116
Record Date Completed: 19960116

12/7/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
08666995 95355592 PMID: 7543117
Identification of immunodominant epitopes in the core and non-structural region of hepatitis C virus by enzyme immunoassay using synthetic peptides.
Park H J; Byun S M; Ha Y J; Ahn J S; Moon H M
Department of Life Science, Korea Advanced Institute of Science and Technology (KAIST), Yusung-gu, Taejon.
Journal of immunoassay (UNITED STATES) May 1995, 16 (2) p167-81, ISSN 0197-1522 Journal Code: 8007167
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Thirty-two synthetic peptides, components of the core and non-structural protein of Hepatitis C virus (HCV), were tested for their reactivities against antibodies in sera of healthy, HCV antibody positive of chronic liver disease patients. Among them, 8 of the core peptides, 4 of the NS4 peptides and 3 of the NS5 peptides reacted with the HCV infected sera. In particular, C22 (core peptide) and NS4-1924 (NS4 peptide) were most reactive with the serum samples giving a positive signal with commercially available enzyme-linked immunosorbent assay (ELISA) kit. Our results indicate that the immunodominant regions of the HCV-derived proteins are located at three regions in the core protein, three regions in the NS4 protein, and one region in the NS5 protein. These results indicate that the selected peptides are useful antigens in detecting antibodies in the sera from individuals infected with HCV.
Record Date Created: 19950905
Record Date Completed: 19950905

12/7/18 (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
08541954 95230252 PMID: 7536231
Evaluation of a multiple peptide assay for typing of antibodies to the hepatitis C virus: relation to genomic typing by the polymerase chain reaction.
Zhang Z X; Yun Z B; Chen M; Sonnerborg A; Sallberg M
Division of Clinical Virology, Karolinska Institute, Huddinge Hospital, Sweden.
Journal of medical virology (UNITED STATES) Jan 1995, 45 (1) p50-5, ISSN 0146-6615 Journal Code: 7705876
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
A panel of 16 type-specific synthetic peptides corresponding to variable antigenic regions within the hepatitis C virus (HCV) core, nonstructural 4 (NS4), and NS5 proteins was synthesised. The peptide panel was used to develop an enzyme immunoassay (EIA) for the detection of antibodies directed to HCV type 1 (genotypes I/1a and II/1b), type 2 (genotypes III/2a and IV/2b), and type 3 (genotype V/3). The peptides corresponded to residues 68-81 of the HCV core (types 1, 2, and 3), residues 1692-1705 and 1710-1728 of HCV NS4 (types 1a, 1b, 2a, 2b, and 3), and residues 2303-2319 of HCV NS5 (types 1a, 1b, 2a, and 2b). The 16-peptide panel was evaluated using human sera from 46 carriers of HCV, which were genotyped in parallel by the polymerase chain reaction (PCR) using primers specific for types I, II, III, IV, and V of HCV core. Of the 46 carriers, 14 (30%) were infected

by HCV genotype I, 7 (15%) by genotype II, 16 (35%) by HCV genotype IV, and 6 (13%) by HCV of genotype V. Two carriers had double infections of types I and II, and the HCV strain of one carrier could not be genotyped. Using the serotyping system, 40 (89%) out of the 45 genotyped carriers were found to contain type-specific antibodies corresponding to the genotypes identified by PCR. In 5 of the 23 carriers infected by genotypes I and/or II, antibodies specific for HCV type 1 could not be detected, whereas all 16 carriers infected by genotype IV were serologically typed as type 2.(ABSTRACT TRUNCATED AT 250 WORDS)
Record Date Created: 19950518
Record Date Completed: 19950518

12/7/20 (Item 20 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08445039 95133207 PMID: 7530398
Linear B-cell epitopes of the NS3-NS4-NS5 proteins of the hepatitis C virus as modeled with synthetic peptides.
Khudyakov Yu E; Khudyakova N S; Jue D L; Lambert S B; Fang S; Fields H A
Hepatitis Branch, Centers for Disease Control and Prevention, Atlanta, Georgia 30333.
Virology (UNITED STATES) Jan 10 1995, 206 (1) p666-72, ISSN 0042-6822 Journal Code: 0110674
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
A set of 150 synthetic peptides spanning the proteins NS3-NS4-NS5 of the hepatitis C virus (HCV) was synthesized and tested with a panel of 20 sera obtained from HCV-infected patients. Of 62 peptides prepared from the NS3 region, none exhibited strong antigenic reactivity. Rather, five peptides from this region demonstrated specific reactivity with only 5-10% of anti-HVC-positive sera. Nonetheless, it is well known that the NS3 region contains strong antigenic epitopes. These epitopes appear to be modeled in a functionally active manner with recombinant proteins and cannot be mimicked properly with short synthetic peptides. This finding suggests that the major NS3 antigenic epitopes are conformationally dependent. Seven of 20 peptides prepared from the NS4 region were immunoreactive. Five peptides from this region demonstrated very strong HCV-specific antigenic reactivity. Four of the five peptides belong to the recognized immunoreactive 5-1-1 region located inside the C100-3 antigen. One peptide demonstrating immunoreactivity with approximately 90% of anti-HCV-positive sera was found outside the C100-3 region at the C-terminal part of the NS4 protein. Of 68 peptides synthesized from the NS5 protein, 30 were immunoreactive. Six of the 30 demonstrated immunoreactivity with 35-50% of anti-HCV-positive sera. Thus, the NS4 and NS5 regions of the HCV polyprotein contain a large number of specific, broadly reactive, linear antigenic epitopes. The highly antigenic reactivity of the NS5 region suggests that this protein may have significant diagnostic potential.
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$18.48 Estimated cost this search
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